

Amendments to the Specification

Please amend the Specification as follows:

Replace the paragraph that begins at line 20 of page 5 and ends at line 7 of page 6 with the following paragraph:

The present invention relates to methods for cleaving IAP, both *in vivo* and *in vitro*, wherein an Omi family polypeptide or polynucleotide sequence is used to promote the cleavage of IAP. In particular, the present invention relates to an active Omi polypeptide that cleaves IAP and renders it non-functional. The Omi family polypeptides will include Omi wild type (WT) sequences and mutant versions, which cleave IAP. Among the available mutant Omi family polypeptides are Omi Δ PDZ, SEQ ID NOs. 48 – 51, 56, 57, 60 – 63, and 66-75 and Omi Δ AVPS, SEQ ID NOs. 52 and 53. Additionally, an Omi catalytic triad may be used to cleave IAP.

Related to the polypeptides are nucleic acid sequences, which express the polypeptides. Various methods can be used to deliver the Omi nucleic acid sequences, or polynucleotides, or the Omi polypeptides. Additionally, mutant versions can be used to block or inhibit Omi WT from cleaving IAP. In particular, an AVPS small molecule can be developed, which inhibits the binding of Omi WT, for example, to an IAP.

Replace the paragraph that begins at line 21 of page 10 and ends at line 22 of page 10 with the following paragraph:

~~Fig. 1 relates~~ Figs. 1A-1E relate to Omi cleavage of IAP proteins, different IAP proteins were incubated in the absence or presence of various amounts of Omi WT or the protease dead mutant Omi SA;

Replace the paragraph that begins at line 18 of page 11 and ends at line 19 of page 11 with the following paragraph:

~~Fig. 2 shows~~ Figs. 2A-2D show Omi/HtrA2 Cleavage of cIAP1 and the relation to the AVPS IAP binding motif;

Replace the paragraph that begins at line 1 of page 12 and ends at line 4 of page 12 with the following paragraph:

Fig. 2B shows the cleavage of cIAP1 by various Omi proteins; 50 nM of cIAP was incubated with 2.5 nM of Omi WT (lane 2), varying amounts of Omi Δ 8 mutant (lanes 3-7) or Omi Δ PDZ mutant (lanes 8-12) in a final volume of 50 μ l PBST, the asterisk (*) in ~~panel B~~ Fig. 2 indicates a cleavage product produced exclusively by Omi Δ PDZ proteolysis of cIAP1;

Replace the paragraph that begins at line 7 of page 12 and ends at line 10 of page 12 with the following paragraph:

Fig. 2D shows the cleavage of β -casein by various Omi proteins; 200 nM of β -casein which was incubated with 2.5 nM of Omi WT (lane 2), varying amounts of Omi Δ 8 mutant (lanes 3-7) or Omi Δ PDZ mutant (lanes 8-12) in a final volume of 50 μ l PBST, ~~the asterisk (*) in panel B indicates a cleavage product produced exclusively by Omi Δ PDZ proteolysis of β -casein;~~

Replace the paragraph that begins at line 11 of page 12 and ends at line 12 of page 12 with the following paragraph:

~~Fig. 3 shows~~ Figs. 3A and 3B show cIAP1 cleavage by Omi/HtrA2 and how cleavage reduces cIAP1's caspase inhibitory activity;

Replace the paragraph that begins at line 20 of page 12 and ends at line 21 of page 12 with the following paragraph:

~~Fig. 4 shows~~ Figs. 4A and 4B show that cIAP1 cleavage by Omi/HtrA2 attenuates its Ub ligase activity on caspase substrates;

Replace the paragraph that begins at line 9 of page 13 and ends at line 14 of page 13 with the following paragraph:

Figs. 4B and 4C show assay for the Ub ligase activity of cIAP1 before and after cleavage, the substrates caspase-3 (400 nM, ~~Panel Fig. 4B~~) and caspase-9 (400 nM, ~~Panel Fig. 4C~~) were incubated with varying concentrations of either full length or Omi-cleaved cIAP1 (25-150 nM) in a 20- μ l reaction volume under the same assay conditions as described in ~~panel Fig. 4A of this figure~~, the ubiquitination on caspase substrates was subsequently checked by immunoblotting, using either an antibody against caspase-3 (~~Panel Fig. 4B~~) or caspase-9 (~~Panel Fig. 4C~~);

Replace the paragraph at line 15 of page 13 with the following paragraph:

~~Fig. 5 shows~~ Figs. 5A and 5B show mapping of Omi/HtrA2 cleavage sites on cIAP1;

Replace the paragraph that begins at line 16 of page 13 and ends at line 2 of page 14 with the following paragraph:

Fig. 5A shows the results of incubating about 5 μ g of full-length cIAP1 (GST-fused) with 0.4 μ g of Omi WT, the cleaved cIAP1 sample, together with Omi (lane 2), the full-length cIAP1 alone (lane 1), and Omi alone (lane 3) were subjected to electrophoresis on a 7.5-20% linear gradient gel, four cleavage polypeptide fragments (~~panel A, F1-F4~~) were generated, 10 pmol of each fragment was excised and subjected to N-terminal sequencing by the Edman Degradation method, the two 30 kDa polypeptides in lane 2 are GST as determined by N-terminal sequencing, several degraded polypeptide bands are already in the full-length cIAP1 preparation, such as that labeled with an asterisk (*), amino acid sequencing confirmed that this band was a fragment of cIAP1 starting from Serine 147, and identical to the band appearing in the OmiWT-treated sample (labeled with an arrow plus an asterisk);

Replace the paragraph that begins at line 9 of page 14 and ends at line 10 of page 14 with the following paragraph:

~~Fig. 6 shows~~ Figs. 6A - 6D show that Omi cleaves cIAP1 in cells, and this cleavage promotes caspase activation in etoposide-induced cell death;

Replace pages 77 through 80 with the following:

All references cited in the preceding text of the patent application or in the following reference list, to the extent that they provide exemplary, procedural, or other details supplementary to those set forth herein, are specifically incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

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